Conclusions: This original radiotherapy regimen delivering only a single stereotactic dose per week seems to be highly feasible with an interesting high rate of efficacy for patients with oligometastases from different solid tumors. Overall, the once weekly treatment is very compliant in advanced cancer stage especially for elderly and frail patients.

POSTER: CLINICAL TRACK: STEREOTACTIC RT

PO-0744

re-EBRT for prostate cancer local relapse after radical, post-operative or salvage RT: toxicities and outcome

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Purpose/Objective: To retrospectively evaluate external beam re-irradiation (re-EBRT), delivered to the prostate or prostatic bed for local recurrence after radical or post-operative/salvage radiotherapy.
Materials and Methods: 17 pts have been treated with re-EBRT at our Department between 2/2008 and 8/2012. Previously RT included radical RT 13 pts (12 pts with EBRT and 1 pt with brachytherapy, post-operative RT (2 pts) or salvage RT (1 pt), 1 pt not reported. All pts had local relapse in the prostate or prostatic bed with no distant metastasis: biopsy was performed in all but 1 pts, and all the pts had total body computer tomography (CT) or ^{11}C-choline positron emission tomography scan. One pt. was previously treated also with 3D-CRT for lymph node recurrence with complete remission.
The mean age, iPSA and Gleason Score (GS) at diagnosis were 61 yrs (49-67), 15 ng/ml (4.57-67) and 6 (4-9), respectively.
The re-EBRT technique included 3D IGRT, stereotactic RT, IMRT, stereotactic RT + IMRT, CyberKnife respectively in 1,8,6,1,1 pts. The following schedules were employed: 25 Gy/5 fr(12 pts), 30 Gy/6 fr(4 pts) and 15 Gy/3 fr (1 pt). Four pts were included in a previous study. Concomitant hormonal therapy (HT) was administered in 7 pts. Toxicity and tumor response were evaluated using Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer and Response Evaluation **Criteria** In Solid Tumors criteria. Biochemical and clinical response, using radiologic criteria, was also registered.
Results: Acute toxicity included: 3 G1, 1 G2 genitourinary events; 1 G1, 1 G2 gastrointestinal events. Late toxicities (> 6 months of f.u., data available in 9 pts): 5 pts with no toxicity; 2 G1 gastrointestinal and 1 G1 genitourinary events respectively.
The mean interval between the primary treatment and the clinical local relapse was 64 months, and the mean follow-up after re-EBRT was 24 months (5-30). Two pts died for the prostate cancer progression at distant sites: the interval between re-EBRT and the death was 30 mo. for each. The remaining 15 patients are alive: 12 with no evidence of disease and 3 pt is alive with disease in clinical control with HT.
Conclusions: In our single institution preliminary experience re-EBRT of local relapse of the prostate cancer appears feasible and well tolerated. Local control was excellent (non local recurrence was registered within mean follow-up of 2 years) and 70% of patients alive with non evidence of disease. Longer follow-up and bigger patient series is warranted in order to confirm these promising early findings.

PO-0745

FFF delivered SBRT in the treatment of lymph node oligometastates: feasibility and early clinical results

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Purpose/Objective: While research in the physics domain for Flattening Filter Free Beams (FFF) beams is increasing, there are few clinical data of FFF beams in clinical practice. Here we reported early clinical results of SBRT and FFF delivery in isolated lymph node oligometastatic patients.
Materials and Methods: Between October 2010 and March 2012, 34 patients were treated with SBRT for oligometastatic lymph node metastasis using Volumetric Modulated Arc Therapy (RapidArc on Truebeam platform). We retrospectively evaluated a total of 25 patients for isolated lymph node metastases in abdomen and/or pelvis treated with SBRT and FFF (28 treatments). Prescription doses were 45 Gy in 6 consecutive fractions of 7.5 Gy for all 28 treatments. The inclusion criteria were: age≥18years, WHO performance status ≤ 2, histologically-proven of primary cancer disease, M1 stage with primary cancer site radically treated with complete response/resection or stable, no other site of disease in progression (amaximum of 3 lymph node sites of disease to treat), diameter of lymph node Target less than 5 cm, Abdomen/pelvic site, no previous surgery or RT in the region to treat, obtained informed consent. Chemotherapy, when prescribed, was interrupted from 20 days before the simulation to the first evaluation after the end of SBRT treatment, as scheduled. Acute toxicity was recorded and scored according to CTCAE v.4. Local control evaluation was scored by means of CT scan and/or PET scan, according to PERCIST criteria.
Results: All 25 FFF SBRT patients completed the treatment. Acute gastrointestinal toxicity was minimal: one patient showed Grade 1 gastrointestinal toxicity.Three other patients presented Grade 2 toxicity. No Grade 3 or higher was recorded. All toxicities were recovered within one week. The preliminary clinical results at the median follow up of 195 days are: complete response in 12 cases, partial response in 11, stable disease in 5, with an overall response rate of 82%; no local progression was recorded.
Conclusions: Data of acute toxicity are excellent for patients treated with SBRT with VMAT using FFF beams. Preliminary clinical results showed a high rate of local control in irradiated lesion. Further data and longer follow up are needed to assess late toxicity and definitive clinical outcomes.

PO-0746

Consequential effects of ablative ionizing radiation on tumor stromal fibroblasts from lung tumors

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Purpose/Objective: Cancer-Associated Fibroblasts (CAFs) are major components of solid malignancies and play central roles on cancer sustainability. In the context of radiotherapy, collateral effects of ablative ionizing radiation (AIR) on stromal components of tumors remain understudied. In this work we have examined the impact of AIR on CAFs from human lung tumors.
Materials and Methods: CAFs prepared from resected human lung tumors were exposed to AIR (1x18Gy). Intrinsic radio-sensitivity was evaluated by checking viability and extent of DNA-damage responses at scalating radiation doses. Proliferation, migration and invasion rates were monitored in label-free assays by xCELLigence system. Inflammatory mediators, as well as regulators of angiogenesis and tumor growth were analyzed by multiplex protein assasy in conditioned medium (CM) from irradiated and control CAFs. Additionally the entire secretory protein profile was examined by mass spectometry. In functional assasys, the potential effects of CAFs released factors on the proliferative and migratory capacity of lung tumor cell (H520 and H522) and on endothelial cells (HUVEC) was also investigated.
Results: Our results show that CAFs survive ablative doses of radiation, but cells enter a senescent state associated with reduced proliferation and invasion. A lowered MMP-1 expression and the stabilization of focal contacts via integrins were responsable mechanisms behind the reduced cell motility. On the other hand, analyses of the secretory profile revealed a reduced expression of angiogenic factors like SDF-1a and TSP-2, and altered expression of tumor regulators such as bFGF, PEDF and MIF upon radiation. No prominensignificant differences were observed on the behaviour of tumor cells or endothelial cells exposed to irradiated and control CAF-CM
Conclusions: AIR provoked a reduction in the proliferative and migratory abilities of CAFs, along with a transformation of their secretory profile. These radiation-induced chages on tumor resident fibroblasts could influence the behaviour of adjacent cells in the tumor tissue and hence influence therapeutic outcomes. Downstream consequences of the changes observed in this study merits further investigations.

PO-0747

Analysis of radiation effects after stereotactic radiotherapy of brain metastases using MRI cine-loops.

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Purpose/Objective: Stereotactic radiotherapy (SRT) of brain metastasis can lead to lesion growth after varying time intervals. The pathophysiology of this radiation effect, that has to be distinguished from regrowth of the tumor, is not well understood. We made cine-loops of serial MRI scans of patients with this effect in order to describe the evolution of SRT associated changes.
Materials and Methods: Ten patients who had received SRT of brain metastases were selected from our departmental database. They had been treated on a Novalis (Brainlab, Feldkirchen, Germany). Patients received either single doses of 21Gy or 18Gy or three doses of 8Gy. Selection criteria for this study were: lesion growth after SRT not caused by tumor progression and the availability of at least five three-monthly follow-up MRI scans. For the cine-loops we used post-gadolinium 3D T1 weighted images. These MRI scans were co-registered using iPlan 4.5 (Brainlab). From the pre-SRT MRI the axial slice with the largest lesion diameter was selected. For the cine-loop we copied the corresponding follow-up MRI images into Microsoft Windows Movie Maker (Microsoft Corp. Redmond USA), put them in chronological order and used the fading mode for the transitions between the separate slices. The ten MRI cine loops were interpreted in a joint meeting of the authors.
Results: In all patients the cine-loops were found to be superior to the separate MRI's for describing and interpreting the events after SRT. The sequence of events showed a similar pattern in all patients, but the timing of the observed events varied. In the movies we saw partial or complete regression of the metastasis first, followed by an enlarging area of contrast enhancement in the surrounding brain tissue. In five patients the volume of this enhancement eventually decreased. Histological examination of the enhancing tissue was possible in two patients and confirmed the existence of radiation necrosis without residual tumor.
Conclusions: Cine-loop MRI analysis enabled better understanding of the changes that develop in follow-up MRI scans after SRT of brain metastases. The cine-loops showed a typical growth pattern after SRT with a gradually expanding area of contrast enhancement in the brain tissue surrounding the shrinking metastasis.

PO-0748

Radiation-induced toxicity in patients receiving stereotactic body radiotherapy for lung tumors

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Purpose/Objective: To analyze the toxicity of hypofractionated lung SBRT according to QUANTEC recommendations.
Materials and Methods: From 2002 to 2010, 44 (25 male, 19 female) patients with small primary lung cancer or oligometastasis were treated with several hypo-fractionation schemes of SBRT at our institution. All patients were immobilized using a stereotactic body frame, simulated with CT scan and treated with multiple static 6 MV beams. A total of 48 lesions were treated, among which 2 patients had 2 lesions and 1 patient had 3 lesions. The median follow-up was 12 months. We exported the composite dose volume histograms (DVHs) of gross target volume (GTV), planning target volume (PTV) and normal lung tissue (whole lung-GTV). For each patient, normal tissue complication probability (NTCP) based on the Poisson model was calculated using the normal lung DVH, and normalized total dose (NTD) volume histograms were generated at 2Gy fractions with a/b = 3.7 Gy to account for different fractionations. Mean dose and V20 (%volume receiving 20Gy) of GTV, PTV and normal lung derived from DVH/NTDVH were correlated with clinical follow-up. Variable importance for projection (VIP) and correlation coefficient (R) were calculated for each variable using partial least squares regression (PLSR) and logistic regression (LR) to identify the prediction factors for normal tissue complications.
Results: There were 2 (4.2%) local failures, 4 (9.1%) grade 2 pneumonitis and 3 (6.8%) radiation-induced fibrosis. The <10% pneumonitis rate is in line with the QUANTEC report for lung SBRT. 5/14 (35.7%) of the lesions in right lower lobe developed complications, in comparison to 1/16 (6.3%) in right upper and middle lobes, 0/5 (0%) in left lower lobe and 1/11 (9.1%) in left upper lobe. The most influential VIP for predicting the complications were mean GTV dose (VIP =1.500, R=0.145) and GTV volume (VIP=1.451, R=-0.140), followed by NTCP (VIP=1.106,R=0.107) although the calculated probability was much higher than the frequency of complications. LR was able to produce a reasonable NTCP curve for these three variables. The prediction factors used for conventional lung RT complications, i.e., V20, VNTD20, mean dose and mean NTD of normal lung had only moderate or low VIP (<0.894), were negatively correlated (R between -0.044 and -0.086) and could not be fit to a NTCP logistic curve.
Conclusions: Radiation induced complication for SBRT increases with the mean GTV dose and cannot be predicted with the known prediction factors for conventional lung RT. The cause for higher probability of complications for right lower lobe is unclear and needs further investigations. NTCP based on Poisson model might be applied to lung SBRT but requires different modeling parameters than that used for conventional lung RT.

PO-0749

Stereotactic body radiation therapy for liver tumors with or without rotational IMRT

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Purpose/Objective: To evaluate the feasibility and efficacy of Stereotactic body radiation therapy (SBRT) for primary liver lesions and liver metastases treated with linear accelerators.
Materials and Methods: Patients with either hepatocellular carcinoma, cholangiocarcinoma or metastatic liver lesions who had one to three lesions treated with SBRT in a single institution were retrospectively reviewed. Tumor response was evaluated according to EASL criteria 3 months after SBRT completion using MRI and/or abdominal CT scan. Responses were categorised as: Stable Disease (SD), Partial Response (PR),Complete Response (CR), Local Progression or Distant Progression in cases of new intra-hepatic lesions out-of-field or extra-hepatic metastases. Local Control (LC), Progression Free Survival (PFS), Overall Survival (OS) and treatment-related toxicities are reported.
Results: Between 2007 and 2012, 20 patients with a total of 24 lesions were treated with SBRT. Fourteen patients presented hepatocellular carcinoma (HCC), the others had either metastatic lesions from colorectal cancer (CRC) or cholangiocarcinoma. The median diameter of the lesions was 23 mm (5-98). The dose per fraction ranged from 6 to 20 Gy with a median total dose of 60 Gy (range: 36-60 Gy). The dose was prescribed to the 80% isodose line covering the PTV. The median follow-up was 24 months. The actuarial LC rate was 78% for patients with HCC and 83% for those with adenocarcinoma and cholangiocarcinoma. Median OS was 37 months and OS rates were 88% at 12 and 24months. PFS was 65% and 53% at 6 and 24 months, respectively. Acute grade 3-4 toxicities occurred in 2 patients; a small proportion of the other patients experienced grade 1 or 2 toxicities.
Conclusions: SBRT provides excellent local control with minimal side effects in selected patients.

PO-0750

Stereotactic RT for recurrent breast cancer with internal mammary chain nodes/sternal disease

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Purpose/Objective: Describe Stereotactic Body RadioTherapy (SBRT) technique for treatment of this disease presentation Review Outcomes (Local Control, Overall Survival, and Toxicity)
Materials and Methods: A total of 12 patients were treated with SBRT by the CyberKnife system between August 2009 and July 2012. All patients had initially presented with local/loco-regional disease. Six patients recurred with sternal metastases, six with Internal Mammary Chain (IMC) lymph node metastases. The Baseline Clinical Characteristics of the patients were well matched with respect to Age, Grade, Stage and Receptor Status at presentation. Median age at presentation was 45 years (Range= 30-63 years). Median Disease-Free Interval between presentation and relapse was 3 years (Range 1-38 years). 2 patients that recurred in the Sternum had synchronous distant disease. 7 patients (58%) of the group as a whole were given Chemotherapy as the first treatment at the time of Sternal/IMC node recurrence. 10 patients (83%) had received prior conventional radiotherapy which overlapped with the target site.Median CTV-PTV